



Figure 2. Blast alignment of Pfu (query 1) against Deep Vent (subject 1)

>gi|2494186|sp|Q51334|DPOL PYRSD DNA polymerase (Deep Vent DNA polymerase)  
[Contains: Endonuclease  
PI-PspI (Psp-GDB pol intein)]  
Length = 1312

Score = 816 bits (2109), Expect = 0.0  
Identities = 414/493 (83%), Positives = 459/493 (92%)

Query: 1 MILDVDYITEEGKPVIRLFKKENGKFKIEHDRTFRPYIYALLRDDSKEIEVKKITGERHG 60  
MILD DYITE+GKP+IR+FKKENG+FK+E+DR FRPYIYALL+DDS+I+EV+KIT ERHG  
Sbjct: 1 MILDADYITEDGKPIIRIFKKENGFEKVEYDRNFRPYIYALLKDDSQIDEVRKITAERHG 60

Query: 61 KIVRIVDVEKVEKKFLGKPIVWKLYLEHPQDVPTIREKVRHPAVVDIFEYDIPFAKRY 120  
KIVRI+D EKV KKFLG+PI VW+LY EHPQDVP IR+K+REH AV+DIFEYDIPFAKRY  
Sbjct: 61 KIVRIIDAELKVRKKFLGRPIEVWRLYFEHPQDVPAIRDKIREHSAVIDIFEYDIPFAKRY 120

Query: 121 LIDKGLIPMEGEEELKILAFDIETLYHEGEEFGKGPIMISYADENEAKVITWKNIDLPY 180  
LIDKGLIPMEG+EELK+LAFDIETLYHEGEEF KGPIMISYADE EAKVITWK IDLPY  
Sbjct: 121 LIDKGLIPMEGDEELKLLAFDIETLYHEGEEFAKGPIMISYADEEEAKVITWKKIDLPY 180

Query: 181 VEVVSSSEREMIKRFLRIIREKDPDIIVTYNGDSFDFPYLAKRAEKLGIKLTIGRDGSEPK 240  
VEVVSSSEREMIKRFL++IREKDPD+I+TYNGDSFD PYL KRAEKLGIKL +GRDGSEPK  
Sbjct: 181 VEVVSSSEREMIKRFLKVIREKDPDVIITYNGDSFDLPYLVKRAEKLGIKLPLGRDGSEPK 240

Query: 241 MQRIGDMTAVEVKGRIHFDLYHVITRTINLPTYTLEAVYEAIFGKPKKEKVYAIEIAKAW 300  
MQR+GDMTAVE+KGRIHFDLYHVI RTINLPTYTLEAVYEAIFGKPKKEKVYA EIA+AW  
Sbjct: 241 MQRIGDMTAVEIKGRIHFDLYHVIRRTINLPTYTLEAVYEAIFGKPKKEKVYAIEIAEAW 300

Query: 301 SGENLERVAKYSMEDAKATYELGKEFLPMEIQLSRLVGQPLWDVSRSTGNLVEWFLLRK 360  
+G+ LERVAKYSMEDAK TYELG+EF PME QLSRLVGQPLWDVSRSTGNLVEW+LLRK  
Sbjct: 301 TGKGLERVAKYSMEDAKVTYELGREFFPMEAQLSRLVGQPLWDVSRSTGNLVEWYLLRK 360

Query: 361 AYERNEVAPNKPSEEEYQRRRLRESYTGGFVKEPEKGLWENIVYLDLFRALYPSIIITHNVS 420  
AYERNE+APNKP E EY+RRRLRESY GG+VKEPEKGLWE +V LDFR+LYPSIIITHNVS  
Sbjct: 361 AYERNEVAPNKPDEREYERRRLRESYAGGYVKEPEKGLWEGLVSLDFRSLYPSIIITHNVS 420

Query: 421 PDTLNLEGCKNYDIAPQVGHKFKCDIPGFIPSLLGHLLEERQKIKTKMKETQDPIEKILL 480  
PDTLN EGC+ YD+AP+VGHKFKCD PGFIPSL LL+ERQ+IK KMK ++DPIEK +L  
Sbjct: 421 PDTLNREGCREYDVAPEVGHKFKCDPFGFIPSLKRLDERQEIKRKMASKDPIEKKML 480

Query: 481 DYRQKAIKLLANS 493  
DYRQ+AIK+LANS  
Sbjct: 481 DYRQRAIKILANS 493

Figure 2--continued. Blast alignment of Pfu (query 1) against Deep Vent (subject 1)

Score = 473 bits (1216), Expect = e-133  
Identities = 248/283 (87%), Positives = 269/283 (94%)

Query: 492 NSFYGYGYAKARWYCKECAESVTAWGRKYIELVWKELEEKFGFKVLYIDTDGLYATIPG 551  
NS+YGYGYAKARWYCKECAESVTAWGR+YIE V KELEEKFGFKVLYIDTDGLYATIPG  
Sbjct: 1029 NSYYGYGYAKARWYCKECAESVTAWGREYIEFVRKELEEKFGFKVLYIDTDGLYATIPG 1088

Query: 552 GESEIKKKALEFVKYINSKLPGLLELEYEGFYKRGFFVTKKRYAVIDEEGKVITRGLEI 611  
+ EEIKKKALEFV YIN+KLPGLLELEYEGFY RGFFVTKK+YA+IDEEGK+ITRGLEI  
Sbjct: 1089 AKPEEIKKKALEFVDYINAKLPGLLELEYEGFYVRGFFVTKKKYALIDEEGKIITRGLEI 1148

Query: 612 VRRDWSEIAKETQARVLETILKHGDVEEAVRIVKEVIQKLANYEIPPEKLAIYEQITRPL 671  
VRRDWSEIAKETQA+VLE ILKHG+VEEAV+IVKEV +KL+ YEIPPEKL IYEQITRPL  
Sbjct: 1149 VRRDWSEIAKETQAKVLEAILKHGNVEEAVKIVKEVTEKLSKYEIPPEKLVIYEQITRPL 1208

Query: 672 HEYKAIGPHVAVAKKLAAGVKIKPGMVIGYIVLRGDGPISNRAILAEEDPKKKHYDAE 731  
HEYKAIGPHVAVAK+LAA+GVK++PGMVIGYIVLRGDGPIS RAILAEE+D +KKHYDAE  
Sbjct: 1209 HEYKAIGPHVAVAKRLAARGVKVRPGMVIGYIVLRGDGPISKRAILAEEDLRKKHYDAE 1268

Query: 732 YYIENQVLPVAVLRILEGFGYRKEDLRYQKTRQVGLTSWLNICK 774  
YYIENQVLPVAVLRILE FGYRKEDLR+QKT+Q GLT+WLNICK  
Sbjct: 1269 YYIENQVLPVAVLRILEAFGYRKEDLRWQTKQTGLTAWLNICK 1311

Figure 3. Assembly of the oligonucleotides into library fragments.

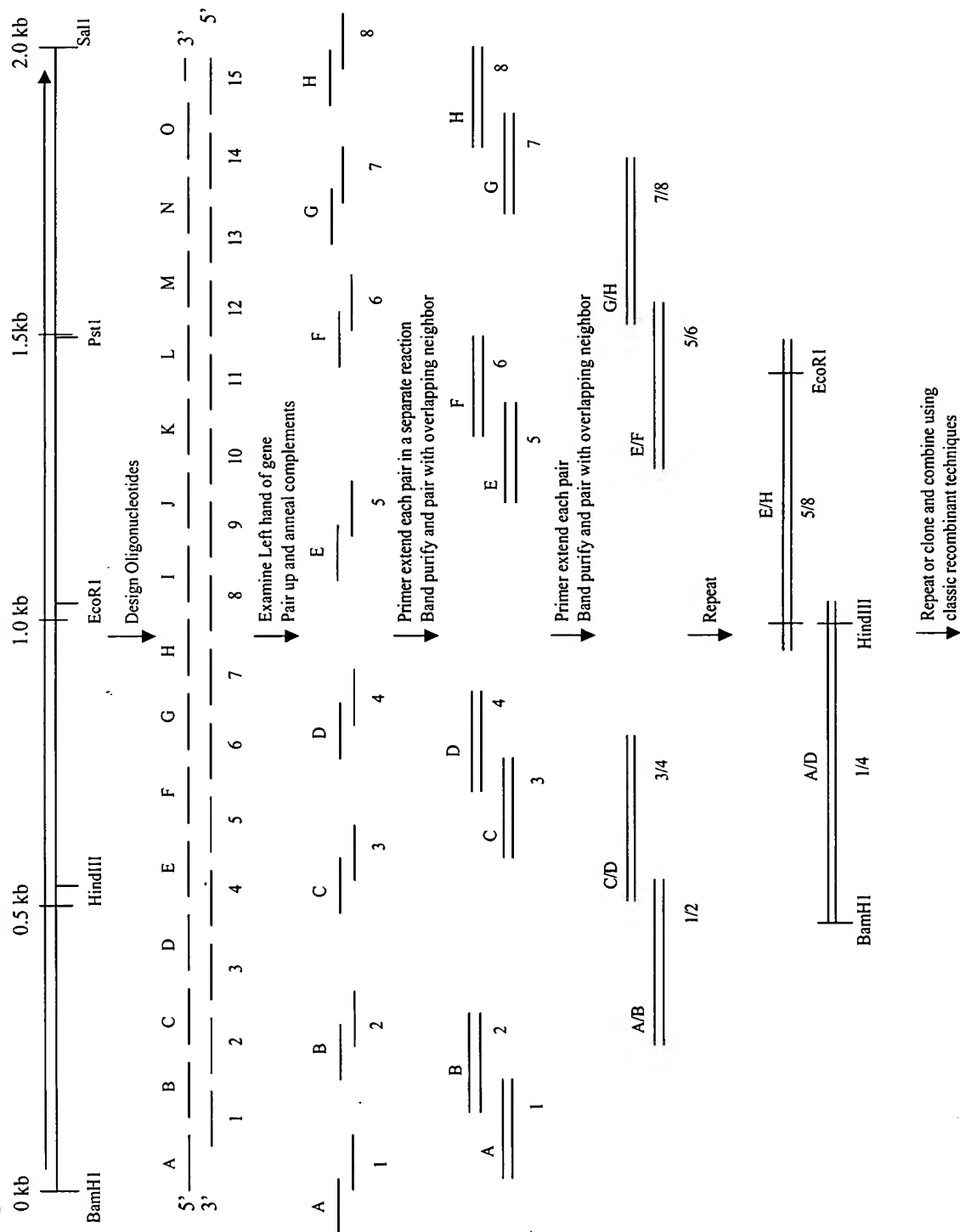


FIG. 4

E coli dut polypeptide sequence:

MKKIDVKILDPRVGKEFPLPTYATSGSAGLDLRACLNDAVELAPGDTTLVPTGLAIHIADPSLAAMMLPRSGLGHKHG  
IVLGNLVGLIDSDYQGQLMISVWNRGQDSFTIQPGERIAQMI FVPVVQAEFNLVEDFDATDRGEGGFHSGRQ

AAD polypeptide sequence:

MSKVILKIKRLPHAQDLPLPSYATPHSSGLDLRAAIEKPLKIKPFERVL IPTGLILEIPEGYEGQVRPRSGLAWKKGL  
TVLNAPGTIDADYRGEVKVILVNLGNEEVVIERGERIAQLVIAPVQRVEVVEVEVSQTQRGEGGFGSTGK

Alignment:

Identities = 61/149 (40%), Positives = 91/149 (60%), Gaps = 1/149 (0%)

Query: 1 MKKIDVKILDPRVGKEFPLPTYATSGSAGLDLRACLNDAVELAPGDTTLVPTGLAIHIAD 60  
M K+ +KI ++ PLP+YAT S+GLDLRA + +++ P + L+PTGL + I +  
Sbjct: 1 MSKVILKIKRLPHAQDLPLPSYATPHSSGLDLRAAIEKPLKIKPFERVL IPTGLILEIPE 60  
Query: 61 PSLAAMMLPRSGLGHKHGIVLGNLVGLIDSDYQGQLMISVWNRGQDSFTIQPGERIAQMI 120  
+ PRSGL K G+ + N G ID+DY+G++ + + N G + I+ GERIAQ++  
Sbjct: 61 -GYEGQVRPRSGLAWKKGLTVLNAPGTIDADYRGEVKVILVNLGNEEVVIERGERIAQLV 119  
Query: 121 FVPVVQAEFNLVEDFDATDRGEGGFHSG 149  
PV + E VE+ T RGEGGFG +G  
Sbjct: 120 IAPVQRVEVVEVEVSQTQRGEGGFGSTG 148

**FIGURE 5**

**5A. Aligned parental sequence showing all possible codons**

**5B. The minimal encoding sequence**

[illegible]

5C. A minimal encoding sequence after the removal of non-similar degeneracies; selection of ADD parent residues at particular sites

[illegible]

| EC | D   | L   | R   | A   | C   | L   | N   | D   | A   | V   | E   | L   | A   | P   | G   | D   | T   | T   | L   | V   | P   | T   | G   | L   | A   | I   | H   | I   | A   | D   | P   |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 31 | GAT | CTG | CGT | CGC | TGC | CTG | AAC | GAT | GCG | GTG | GAA | CTG | GCG | CCG | GGC | GAT | ACC | ACC | CTG | GTG | CCG | ACC | GGC | CTG | GCG | ATT | CAT | ATT | GCG | GAT | CCG |
|    | GAC | TTA | CGC | GCC | TGT | TTA | AAT | GAC | GCC | GTT | GAG | TTA | GCC | CCT | GGT | GAC | ACG | ACG | TTA | GTT | CCT | ACG | GGT | TTA | GCC | ATC | CAC | ATC | GCC | GAC | CCT |
|    | TTG | CGG | GCA |     |     | TTG | GCA | GTC | GCA | GTC |     | TTG | GCA | CCA | GGG |     | ACT | ACT | TTG | GTC | CCA | ACT | GGG | TTG | GCA | ATA |     | ATA | GCA | CCA | CCA |
|    | CTT | CGA | GCT |     |     | CTT | GCT | GTA | GCT | GTA |     | CTT | GCT | CCC | GGA |     | ACA | ACA | CTT | GTA | CCC | ACA | GGA | CTT | GCT |     |     |     | GCT | CCC | CCC |
|    | CTC | AGA |     |     |     | CTC |     |     |     |     |     | CTC |     |     |     |     |     |     | CTC |     |     |     |     | CTC |     |     |     |     |     |     |     |
|    | CTA | AGG |     |     |     | CTA |     |     |     |     |     | CTA |     |     |     |     |     |     | CTA |     |     |     |     | CTA |     |     |     |     |     |     |     |

| AAD | 31 | D   | L   | R   | A   | A   | I   | E   | K   | P   | L   | K   | I   | K   | P   | F   | E   | R   | V   | L   | I   | L   | E   | I   | P   | E   | G   |
|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |    | GAT | CTG | CGT | CGG | CGG | ATT | GAA | AAA | CCG | CTG | AAA | ATT | AAA | CCG | TTT | GAA | CGT | GTG | CTG | ATT | CTG | GAA | ATT | CCG | GAA | GGC |
|     |    | GAC | TTA | CGC | GCC | GCC | ATC | GAG | AAG | CCT | TTA | AAG | ATC | AAG | CCT | TTC | GAG | CGC | GTT | TTA | ATC | TTC | GAG | ATC | CCT | GAG | GGT |
|     |    | TTG | CGG | GCA | GCA | ATA |     |     | ATA | CCA | TTG |     |     |     | CCC |     |     | CGG | GTC | TTG | ATA | CCA | ACT | GGG | TTG | ATA | GGG |
|     |    | CTT | CGA | GCT | GCT |     |     |     |     | CCC | CTT |     |     |     |     |     |     | CGA | GTA | CTT |     | CTT |     | CCC |     | GGG |     |
|     |    | CTC | AGA |     |     |     |     |     |     |     | CTC |     |     |     |     |     | AGA |     | CTC |     |     | CTC |     |     |     | GGG |     |
|     |    | CTA | AGG |     |     |     |     |     |     |     | CTA |     |     |     |     |     | AGG |     | CTA |     |     | CTA |     |     |     | GGG |     |

**5B--continued**

[illegible]

**5C--continued**

[illegible]

| EC | 62 | S   | L   | A   | A   | M   | M   | L   | P   | R   | S   | G   | L   | G   | H   | K   | H   | G   | I   | V   | L   | N   | L   | V   | G   | L   | I   | D   | S   | D   | Y   |
|----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |    | AGC | CTG | GCG | GCG | ATG | ATG | CTG | CCG | CGT | AGC | GGC | CTG | GGC | CAT | AAA | CAT | GGC | ATT | GTG | CTG | GGC | CTG | GTG | GGC | CTG | ATT | GAT | AGC | GAT | TAT |
|    |    | TCT | TTA | GCC | GCC |     |     | TTA | CCT | CGC | TCT | GGT | TTA | GGT | CAC | AAG | CAC | GGT | ATC | GTT | TTA | GGT | TTA | GTT | GGT | TTA | ATC | GAC | TCT | GAC | TAC |
|    |    | AGT | TTG | GCA | GCA |     |     | TTG | CCA | CGG | AGT | GGG | TTG | GGG |     |     | GGG | ATA | GTC | TTG | GGG | TTG | GTC | GGG | TTG | ATA |     | AGT |     |     |     |
|    |    | TCA | CTT | GCT | GCT |     |     | CTT | CCC | CGA | TCA | GGA | CTT | GGA |     |     | GGA |     | GTA | CTT | GGA | CTT | GTA | GGA | CTT |     | TCA |     |     |     |     |
|    |    | TCC | CTC |     |     |     |     | CTC |     | AGA | TCC | CTC | CTC | CTC |     |     |     |     |     | CTC | CTC | CTC | CTC |     |     |     | TCC |     |     |     |     |
|    |    | TCG | CTA |     |     |     |     | CTA | AGG | TCG | CTA | CTA | CTA | CTA |     |     |     |     |     | CTA | CTA | CTA | CTA |     |     |     | TCG |     |     |     |     |

[illegible]

| Min. Seq. | TCT | CTG | CGG | CGG | ATG | ATG | CTG | CCG | CGT   | AGC | GGC | CTG | GGC | CAT     | AAA | CAT | GGC | ATA | GTG | CTG | GGG | AAC | CTG | GTG | GGC | CTG | ATT | GAT | AGC | GAT | TAT |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|---|-----|-----|-----|-----|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| A         | --- | A   | G   | CA  | G   | G   | G   | G   | CGT <td>AGC</td> <td>GGC</td> <td>CTG</td> <td>GGC</td> <td>CAT</td> <td>AAA</td> <td>CAT</td> <td>GGC</td> <td>ATA</td> <td>GTG</td> <td>CTG</td> <td>GGG</td> <td>AAC</td> <td>CTG</td> <td>GTG</td> <td>GGC</td> <td>CTG</td> <td>ATT</td> <td>GAT</td> <td>AGC</td> <td>GAT</td> <td>TAT</td> | AGC | GGC | CTG | GGC | CAT     | AAA | CAT | GGC | ATA | GTG | CTG | GGG | AAC | CTG | GTG | GGC | CTG | ATT | GAT | AGC | GAT | TAT |
| S         | L   | A   | A   | A   | M   | M   | L   | P   | R   | S   | G   | L   | G   | H       | K   | H   | G   | I   | V   | L   | G   | N   | L   | V   | G   | L   | I   | D   | S   | D   | Y   |
| Y         | -   | E   | G   | Q   | V   | R   | R   | A   | W   | K   | A   | A   | V   | K       | L   | K   | L   | T   | T   | V   | L   | L   | A   | P   | A   | T   | A   | A   |     |     |     |
|           |     |     |     | K   |     |     |     | R   | R   | Q   | R   | V   | V   | Q       | V   | Q   | A   | A   | A   | A   | V   | R   | P   | P   | A   | P   | A   | T   | G   |     |     |
|           |     |     |     | L   |     |     |     |     |   |     |     |     |     | Q, Y, * | N   | N   | M   | M   | M   |     |     |     | V   | L   | M   | M   |     |     |     |     |     |

| TCT | --- | CGC | CGC | CAG | ATG | CTG | CCG | CGT | AGC | GGC | CTG | GGC | TGG | AAA | CAT | GGC | ATA | GTG | CTG | CTG | AAC | CGC | GTG | GGC | CTG | ATT | GAT | AGC | GAT | TAI |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| A   |     | A   | G   | A   | G   | G   | G   | G   | G   | C   |     |     |     | A   | A   | G   | T   | AC  | G   |     |     | CC  |     | AC  |     |     | GC  |     |     |     |
| S   | -   | A   | A   | Q   | M   | L   | P   | R   | S   | G   | L   | G   | W   | K   | H   | G   | I   | V   | L   | L   | N   | A   | V   | G   | L   | I   | D   | S   | D   | Y   |
| Y   |     | E   | G   |     | V   | R   |     |     |     | A   |     |     | A   | K   | Q   |     | L   | T   | V   |     |     | P   | P   | T   |     | A   |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     | N   | N   |     | A   | A   | M   |     |     | L   | M   | P   | T   | G   |     |     |     |     |



[illegible]

5A--continued

ECD 123 V V Q A E F N L V E D F D A T D R G E G G F G H S G R Q 150  
GTG GTG CAG GCG GAA TTT AAC CTG GTG GAA GAT TTT GAT CCG ACC GAT CGT GGC GAA GGC GGC TTT GGC CAT AGC GGC CGT CAG  
GTT GTT CAA GCC GAG TTC AAT TTA GTT GAG GAC TTC GAC GGC ACG GAC CGC GGT GAG GGT GGT TTC GGT CAC TCT GGT CGC CAA  
GTC GTC GCA GCT TTG GTC CTT GTA CTT ACA GCA ACT CGG GGG GGG GGG GGA TCA GGA CGA AGA  
GTA GTA GCT GCT CTC CTA AGG AGG TCC AGG TCG AGG

AAD 122 V Q R V E V V E V E V S Q T Q R G E G G F G S T G T K 149  
GTG CAG CGT GTG GAA GTG GAA GTG GAA GAG GAG GTT GAG GTT GAG GTT TCT AGC AGC CAG CGT GGC GAA GGC GGC TTT GGC ACC ACC AAA  
GTT CAA CGC GTT GAG GTT GAG GTT GAG GTT GAG GTT TCT CAA ACG CAA CGC GGT GAG GGT GGT TTC GGT TCT ACG GGT ACG AAG  
GTC CGG GTC GTC GTC GTA GTC GTA TCA TCA ACA CGG GGG GGG GGG GGA TCA ACA GGA ACA  
GTA GTA GTC GTA GTC GTA TCA TCA ACA CGA GGA GGA GGA TCC TCC  
AGA AGG AGG TCG TCG

5B--continued

Min. Seq. GTG GTG CAG GCG GAA TTT AAT CTG GTG GAA GAT TTT GAT GCG ACC GAT CGT GGC GAA GGC GGC TTT GGC CAT AGC GGC AGA CAG TAA TGA  
CA G T G GT GA A G TC CA C G  
V V Q A E F N L V E D F D A T D R G E G G F G H S G R Q \*  
Q R V V V I Q V S Q Q E P Y  
E L D V Y P H

5C--continued

GTG GTG CAG GCG GAA TTT AAT CTG GTG GAA GAT TTT TCT CAG ACC GAT CGT GGC GAA GGC GGC TTT GGC TCT AGC GGC AGA CAG TAA TGA  
CA G T G GT GA A G C G C A  
V V Q A E F N L V E D F S Q T D R G E G G F G S S G R Q \*  
Q R V V V I Q V E V Q E H  
E L D V

FIGURE 6

**KpnI HindIII NdeI**

1 TT GGTACC AAGCTT CAT ATG A(A/G) (A/C) AAA (A/G)TT (G/A) (A/T)T (G/C)TG AAA 38  
AA CCATGG TTCGAA GTA TAC T(T/C) (T/G) TTT (T/C)AA (C/T) (T/A)A (C/G)AC TTT  
M K/S/R/N K I/V D/I/V/N V/L K

39 ATT (C/A) (T/A)G CGT C(C/T)G C(G/C)T CAT G(G/C)C (A/C)AA GA(A/T) TT(T/A) 69  
TAA (G/T) (A/T)C GCA G(G/A)C G(C/G)A GTA C(C/G)G (T/G)TT CT(T/A) AA(A/T)  
I L/K/Q/M R P/L R/P H G/A K/Q E/D F/L

**StuI**

70 CCG CTG CCG A(C/G)C TAT GCG ACC (T/C)CT CAC AGC (G/T)CA GGC CTG GAT CTG 113  
GGC GAC GGC T(G/C)G ATA CGC TGG (A/G)GA GTG TCG (C/A)GT CCG GAC CTA GAC  
P L P T/S Y A T S/P H S A/S G L D L

114 CGT GCG (T/G) (G/C)C (C/A)TT (A/G)A(C/G) (A/G)A(T/A) (G/C)CG (G/C)TG (G/A)AA  
140  
GCA CGC (A/C) (C/G)G (G/T)AA (T/C)T(G/C) (T/G)T(A/T) (C/G)GC (C/G)AC (C/T)TT  
R A C/A/S/G L/I N/E/K/D D/K/N/E A/P V/L E/K

141 (C/A)TT (G/A) (C/A)G CCG (G/T) (G/T)T GA(T/A) A(C/G)G (A/G) (C/T)G CTG 164  
(G/T)AA (C/T) (G/T)C GGC (C/A) (C/A)A CT(A/T) T(G/C)C (T/C) (G/A)C GAC  
L/I A/K/E/T P G/F/V/C D/E T/R T/V/M/A L

**AgeI**

165 (G/A)TT CCG ACC GGT CTG ATC (A/C)TT (C/G)A(T/A) ATT (G/C)CG GA(T/A) GGT 200  
(C/T)AA GGC TGG CCA GAC TAG (T/G)AA (G/C)T(A/T) TAA (C/G)GC CT(A/T) CCA  
V/I P T G L I I/L H/E/D/Q I A/P D/E G

201 T(C/A)T G(C/A)G G(C/G)G CAG (A/G)TG C(T/G)G CCG CGT AGC GGC CTG G(G/C)C 236  
A(G/T)A C(G/T)C C(G/C)C GTC (T/C)AC G(A/C)C GGC GCA TCG CCG GAC C(C/G)G  
S/Y A/E A/G Q M/V L/R P R S G L G/A

237 TGG AAA (C/A)A(T/G) GGC (A/T)TA (G/A) (T/C)G (C/G)TG CTG AAC GCG 266  
ACC TTT (G/T)T(A/C) CCG (T/A)AT (C/T) (A/G)C (G/C)AC GAC TTG CGC  
W K H/K/Q/N G I/L V/T/A/M L/V L N A

**Clai**

267 (G/C) (T/C)G GGC (C/A) (T/C)G ATC GAT (A/G) (G/C)C GAT TAT C(A/G)G GGC 296  
(C/G) (A/G)C CCG (G/T) (A/G)C TAG CTA (T/C) (C/G)G CTA ATA G(T/C)C CCG  
V/P/A/L G L/T/P/M I D S/A/T/G D Y Q/R G

297 (C/G)AA (C/G)TG A(T/A)G (A/G)TT A(G/T)C (G/C)TG GTG AAC C(G/T)G GGC 326  
(G/C)TT (G/C)AC T(A/T)C (T/C)AA T(C/A)G (C/G)AC CAC TTG G(C/A)C CCG  
Q/E L/V M/K I/V S/I V/L N N R/L G

327 (C/A)A(G/C) GA(T/A) GAA (T/G)TT (A/G) (C/T)G ATT (C/G)AG C(C/G)G GGC GAA 356  
(G/T)T(C/G) CT(A/T) CTT (A/C)AA (T/C) (G/A)C TAA (G/C)TC G(G/C)C CCG CTT  
Q/N/H/K D/E E F/V T/V/M/A I Q/E P/R G E

**FspI**

357 CGT ATT GCG CAG (A/C)TG (A/G)TT (T/A)TT G(T/C)G CCG GTG (G/C) (T/A)G 389  
GCA TAA CGC GTC (T/G)AC (T/C)AA (A/T)AA C(A/G)C GGC CAC (C/G) (A/T)C  
R I A Q M/L I/V F/I V/A P V V/Q/E/L

390 C(A/G)G G(C/T)G GAA (T/G)TT (A/G) (A/T)T (C/G) (T/A)G GTG GAA GA(T/A) 416  
G(T/C)C C(G/A)C CTT (A/C)AA (T/C) (T/A)A (G/C) (A/T)C CAC CTT CT(A/T)  
Q/R A/V E F/V N/V/I/D L/E/Q/V V E D/E

417 (T/G)TT TCT CAG ACC (G/C)A(T/G) CGT GGC GAA GGC GGC TTT GGC TCT A(G/C)C 458  
(A/C)AA AGA GTC TGG (C/G)T(A/C) GCA CCG CTT CCG CCG AAA CCG AGA T(C/G)G  
F/V S Q T D/Q/E/H R G E G G F G S S/T

**BamHI EcoRI**

459 GGC A(G/C)A (C/A)AG TAA TGA GGATCC GAATTC TT 487  
CCG T(C/G)T (G/T)TC ATT ACT CCTAGG CTTAAG AA

Figure 7

10 20 30 40 50 60 70  
TTGGTACCAAGCTTCATATGARMAAARTTRWTSTGAAAATTMWGCCTCYGCSTCATGSCMAAGAWTTWCC  
AACCATGGTTCGAAGTATACTYKTTTTYAAWASACTTTTAAKWCGCAGRCGSAGTACSGKTTCTWAAWGG

80 90 100 110 120 130 140  
GCTGCCGASCATGCGACCYCTCACAGCKCAGGCCTGGATCTGCGTGCGKSCMTTRASRAWSCGSTGRAA  
CGACGGCTSGATACGCTGGRGAGTGTTCGMGTCCGGACCTAGACGCACGMSGKAAYTSYTWSGCSACYTT

150 160 170 180 190 200 210  
MTTRMGCCGKKTGAWASGRYGCTGRTTCCGACCGGTCTGATCMTTSAWATTSCGGAWGGTTMTGMGGSGC  
KAAKCGGCMMACTWTSCYRCGACYAAGGCTGGCCAGACTAGKAASTWTAASGCCTWCCAAKACKCCSCG

220 230 240 250 260 270 280  
AGRTGCKGCCGCTAGCGGCCTGGSCCTGGAAAMAKGGCWTAARYGSTGCTGAACGCGSYGGGCMYGATCGA  
TCYACGMCGGCGCATCGCCGGACCSGACCTTTKTMCCGWATYRCSACGACTTGCGCSRCCCGKRCTTAGCT

290 300 310 320 330 340 350  
TRSCGATTATCRGGGCSAASTGAWGRTTAKCSTGGTGAACCKGGGCMASGAWGAAKTTRYGATTSAGCSG  
AYSGCTAATAGYCCCGSTTSACTWCYAATMGSACCACTTGGMCCCGKTSCTWCTTMAAYRCTAASTCGSC

360 370 380 390 400 410 420  
GGCGAACGTATTGCGCAGMTGRTTWTGCGCCGGTGSWGCRCGGYGGAAKTTRWTSWGGTGGAAGAWKTTT  
CCGCTTGCCATAACGCGTCKACYAAWAACRCGGCCACSWCGYCCRCCTTMAAYWASWCCACCTTCTWMAAA

430 440 450 460 470 480  
CTCAGACCSAKCGTGGCGAAGGCGGCTTTGGCTCTASCGGCASAMAGTAATGAGGATCCGAATTCTT  
GAGTCTGGSTMGCACCGCTTCCGCCGAAACCGAGATSGCCGTSTKTCATTACTCCTAGGCTTAAGAA

Figure 8.

14  
atg atc ctg gat g(t/c)t gac tac atc act gaa ga(a/c) ggc aaa ccg (g/a)tt atc cgt (c/a)t(g/c) ttc  
M I L D V/A D Y I T E E/D G K P V/I I R L/I/M F  
  
aaa aaa gag aac ggc (a/g)aa ttt aag (a/g)tt gag (c/t)at gat cgc a(a/c)c ttt cgt cca tac att tac gct  
K K E N G K/E F K I/V E H/Y D R N/T F R P Y I Y A  
  
ctg ctg a(g/a)a gat gat tct (a/c)ag att ga(g/t) gaa gtt a(g/a)a aaa atc act g(g/c)t gag cgc cat ggc aag att  
L L R/K D D S K/Q I E/D E V K/R K I T G/A E R H G  
K I  
  
214 215  
gtt cgt atc (a/g)tt gat g(t/c)g gaa aag gta (g/a)(g/a)g aag aaa ttt ctg ggc a(a/g)a cca atc (a/g)(a/c)g  
V R I I/V D V/A E K V G/E/R/K K K F L G K/R P I  
K/T/E/A  
  
gtg tgg a(g/a)a ctg tat (c/t)tc gaa cat cca caa gat gtt ccg a(t/c)t att cgc ga(g/t) aaa (g/a)tt cgc  
V W K/R L Y L/F E H P Q D V P T/A I R E/D K V/I R  
  
gaa cat (c/t)ct gca gtt (g/a)tt gac atc ttc gaa tac gat att cca ttt gca aag cgt tac ctc atc gac aaa  
E H P/S A V V/I D I F E Y D I P F A K R Y L I D K  
  
ggc ctg ata cca atg gag ggc ga(g/t) gaa gaa ctc aag (a/c)tc ctg gcg ttc gat ata gaa acc ctc tat  
G L I P M E G E/D E E L K I/L L A F D I E T L Y  
  
cac gaa ggc gaa gag ttt g(g/c)t aaa ggc cca att ata atg att agc tat gca gat gaa (a/g)a(a/c) gaa gca aag  
H E G E E F G/A K G P I I M I S Y A D E K/N/E/D E A  
K  
  
gtg att act tgg aaa aa(a/c) ata gat ctc cca tac gtt gag gtt gta tct tcc gag cgc gag atg att aag cgc  
V I T W K K/N I D L P Y V E V V S S E R E M I K R  
  
ttt ctc a(g/a)a (g/a)tt atc cgc gag aag gat ccg gac (g/a)tt atc (g/a)tt act tat aac ggc gac tct ttt  
F L R/k V/I I R E K D P D V/I I V/I T Y N G D S F  
  
gac (c/t)tc cca tat ctg g(t/c)g aaa cgc gca gaa aaa ctc ggt att aaa ctg (a/c)ct (a/c)tc ggc cgt gat ggt  
D F P Y L V/A K R A E K L G I K L T/P I/L G R D  
G  
  
tcc gag ccg aag atg cag cgt (a/c)tc ggc gat atg acc gct gta gaa (g/a)tt aag ggt cgt atc cat ttc gac  
S E P K M Q R I/L G D M T A V E V/I K G R I H F D  
  
ctg tat cat gta att (a/c)(c/g)c cgt act att aac ctc ccg act tac act ctc gag gct gta tat gaa gca att  
L Y H V I T/S/P/R R T I N L P T Y T L E A V Y E A I  
  
ttt ggt aag ccg aag gag aag gta tac gcc (g/c)at gag att gca (a/g)ag gcg tgg gaa (a/t)cc ggt (a/g)ag  
F G K P K E K V Y A D/H E I A K/E A W E T/S G K/E  
  
(a/g)(a/g)c ctc gag cgt gtt gca aaa tac tcc atg gaa gat gca aag g(t/c)g act tat gaa ctc ggc a(g/a)a gaa ttc  
N/G/D/S L E R V A K Y S M E D A K V/A T Y E L G R/K  
E F

(c/t)tc cca atg gaa (a/g)(t/c)t cag ctc tct cgc ctg gtt ggc caa cca ctg tgg gat gtt tct cgt tct tcc  
L/F P M E I/T/V/A Q L S R L V G Q P L W D V S R S S

acc ggt aac ctc gta gag tgg t(t/a)t ctc ctg cgc aaa gcg tac gaa cgc aac gaa (g/c)tg gct ccg aac aag  
T G N L V E W F/Y L L R K A Y E R N E V/L A P N K

cca (t/g)(c/a)c gaa (c/g)(g/a)a gag tat (c/g)aa cgc cgt ctc cgc gag tct tac (a/g)ct ggt ggc t(t/a)t  
P S/Y/A/D E R/Q/G/E E Y Q/E R R L R E S Y T/A G G F/Y

gtt aaa gag cca gaa aag ggc ctc tgg gaa (a/g)(a/g)c (a/c)tc gtg t(c/a)c ctc gat ttt cgc (g/t)ct ctg  
V K E P E K G L W E N/S/D/G I/L V Y/S L D F R A/S L

tat ccg tct att atc att acc cac aac gtg tct ccg gat act ctc aac c(t/g)c gag ggc tgc a(g/a)a  
Y P S I I I T H N V S P D T L N L/R E G C K/R

(a/g)a(a/c) tat gat (g/a)tt gct ccg (c/g)aa gta ggc cac aag ttc tgc aag gac (a/t)tc ccg ggc ttt att  
K/N/E/D Y D V/I A P Q/E V G H K F C K D I/F P G F I

ccg tct ctc ctg (a/g)(a/g)g c(a/g)t ctg ctc ga(g/t) gaa cgc caa (a/g)ag att aag (a/c)(g/c)c aaa atg aag  
P S L L K/R/B/G R/H L L E/D E R Q K/E I K T/S/P/R K M K

g(a/c)g (a/t)cc (c/a)ag gat ccg att gaa aaa a(t/a)a (a/c)tg ctc gac tat cgc caa a(g/a)a gcg att aaa  
E/A T/S Q/K D P I E K I/K M/L L D Y R Q R/K A I K

(a/c)tc ctc gca aac tct t(a/t)t tac ggc tat tat ggc tat gca aaa gca cgc tgg tac tgt aag gag tgt gct  
L/I L A N S F/Y Y G Y Y G Y A K A R W Y C K E C A

gag tcc gtt act gct tgg ggt cgc (a/g)aa tac atc gag (c/t)tc gtg (t/c)gg aag gag ctc gaa gaa aag ttt ggc  
E S V T A W G R K/E Y I E L/F V W/R K E L E E K F G

ttt aaa gtt ctc tac att gac act gat ggt ctc tat gcg act att ccg ggt g(g/c)t (a/g)ag (c/t)ct gag  
F K V L Y I D T D G L Y A T I P G G/A E/K S/P E

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gaa att aag aaa aag gct ctc gaa ttt gtg aaa tac att aac (g/t)cg aag ctc ccg ggt ctc ctg gag ctc gaa  
E I K K K A L E F V K(D) Y I N A/S K L P G L L E L E

tat gaa ggc ttt tat (g/a)(t/a)g cgc ggc ttc ttc gtt acc aag aag a(g/a)a tat gcg (g/c)tg att gat gaa gaa  
Y E G F Y V/E/M/K R G F F V T K K R/K Y A V/L I D E E

ggc aaa (g/a)tt att act cgt ggt ctc gag att gtg cgc cgt gat tgg agc gaa att gcg aaa gaa act caa gct  
G K V/I I T R G L E I V R R D W S E I A K E T Q A

a(g/a)a gtt ctc gag (a/g)ct att ctc aaa cac ggc (g/a)ac gtt gaa gaa gct gtg a(g/a)a att gta aaa gaa gta  
R/K V L E T/A I L K H G D/N V E E A V R/K I V K E V

a(t/c)c (c/g)aa aag ctc (g/t)ct aa(a/c) tat gaa att ccg cca gag aag ctc g(t/c)g att tat gag cag att  
I/T Q/E K L A/S K/N Y E I P P E K L V/A I Y E Q I

act cgc ccg ctg cat gag tat aag gcg att ggt ccg cac gtg gct gtt gca aag a(g/a)a ctg gct gct a(g/a)a ggc gtg  
T R P L H E Y K A I G P H V A V A K R/K L A A K/R G V

aaa (g/a)tt a(g/a)a ccg ggt atg gta att ggc tac att gta ctc cgc ggc gat ggt ccg att agc aa(a/c) cgt gca  
K V/I R/K P G M V I G Y I V L R G D G P I S K/N R A

att cta gct gag gaa t(t/a)c gat c(c/t)g a(g/a)a aag cac aag tat gac gca gaa tat tac att gag aac cag gtg  
I L A E E F/Y D P/L K/R K H K Y D A E Y Y I E N Q V  
2272 2273  
ctc ccg gcg gta ctc cgt att ctg gag g(g/c)t ttt ggc tac cgt aag gaa gac ctc cgc t(a/g)(c/g) caa aag  
L P A V L R I L E G/A F G Y R K E D L R Y/W/\*C Q K  
act a(g/a)a cag (g/a)(t/c)t ggc ctc act (g/t)ct tgg ctc aac att aaa aaa tcc ggt acc cac tag tgc tag cat gac  
T K/R Q V/A/I/T G L T A/S W L N I K K S G T H \*

Figure 9. A comparison of the polymerase to 3' to 5' exonuclease activity

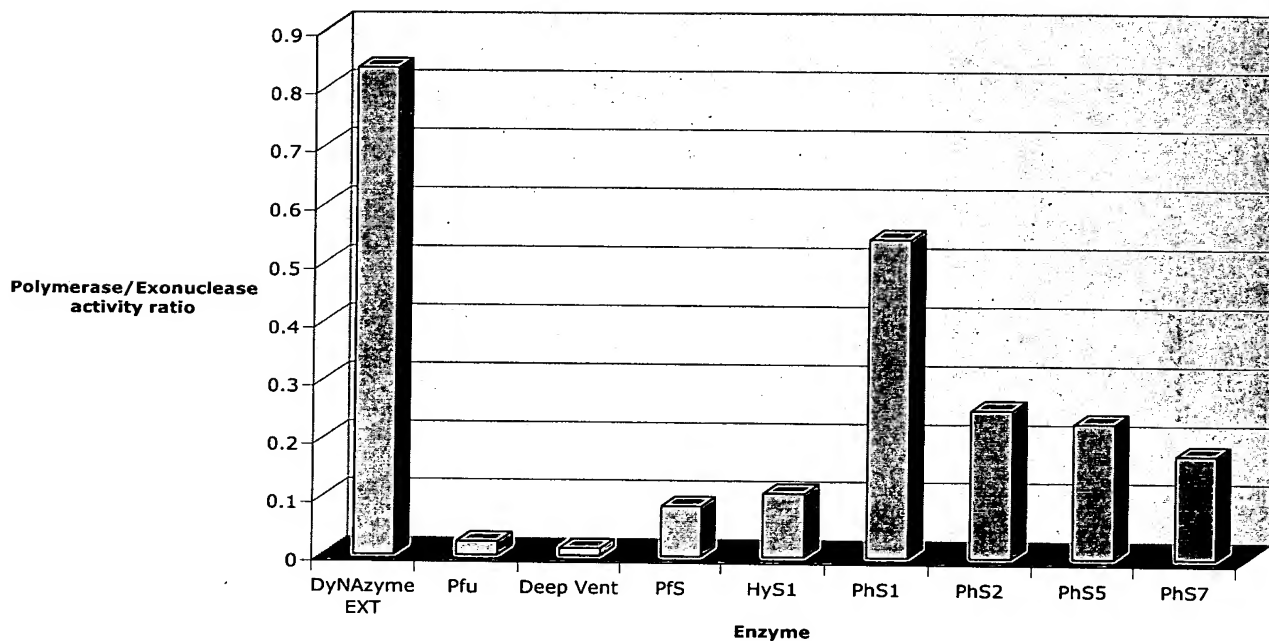
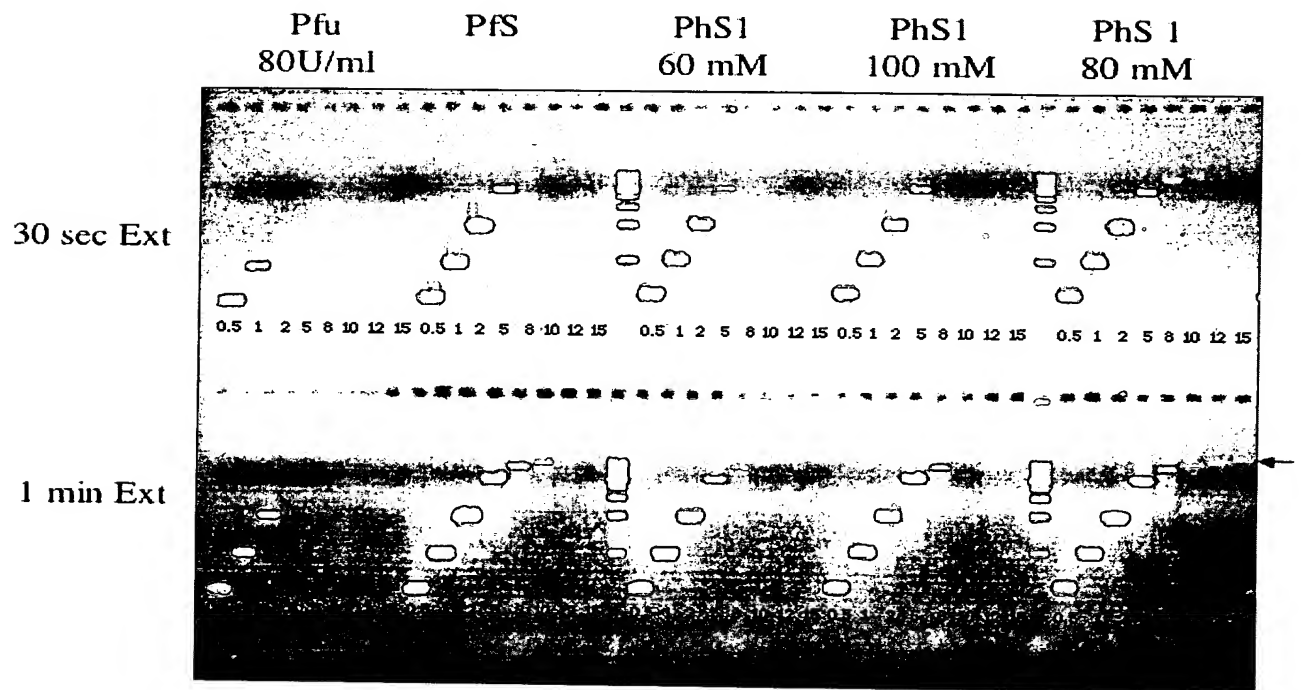




FIGURE 10



|               | 10        | 20                          | 30  | 40                                | 50                                | 60        |
|---------------|-----------|-----------------------------|---|-----------------------------------|-----------------------------------|-----------|
| pfu           | M I L D V | E G K P V I R L F           | K K E N G F K K I I E                       | H D R R I T F R P Y I             | A L L R D D S K I E V K K I T     | G E R H G |
| DeepVent      | M I L D A | D Y I T E D G K P I I R I T | F K K E N G E F K K I I E                   | H D R R I T F R P Y I             | A L L R D D S Q I D E V R K K I T | A E R H G |
| Hybrid_design | M I L D X | D Y I T E X G K P X I R I X | F K K E N G X F K X E X D R R I T F R P Y I | A L L X D D S X I X E V R X K I T | X E R H G                         |           |
| HyS1          | M I L D A | D Y I T E D G K P V I R L F | K K E N G E F K K I I E                     | Y D R T F R P Y I                 | A L L R D D S K I E V R K K I T   | A E R H G |
| Hyb2          | M I L D A | D Y I T E E G K P V I R I T | F K K E N G E F K V E Y D R N               | F R P Y I                         | A L L E D D S K I D E V R K K I T | A E R H G |
| Hyb3          | M I L D A | D Y I T E E G K P V I R I F | K K E N G E F K V E Y D R N                 | F R P Y I                         | A L L E D D S K I D E V R K K I T | A E R H G |
| HyS4          | M I L D A | D Y I T E E G K P V I R I F | K K E N G E F K V E Y D R N                 | F R P Y I                         | A L L E D D S K I D E V R K K I T | A E R H G |
| PhS1          | M I L D A | D Y I T E E G K P V I R I F | K K E N G E F K I I E H D R R I T F R P Y I | A L L K D D S K I E V K K I T     | A E R H G                         |           |
| PhS2          | M I L D V | D Y I T E E G K P V I R L F | K K E N G E F K V E Y D R T F R P Y I       | A L L K D D S K I D E V R K K I T | G E R H G                         |           |
| PhS3          | M I L D A | D Y I T E E G K P I I R L F | K K E N G E K F K V E Y D R T F R P Y I     | A L L K D D S K I E V R K K I T   | G E R H G                         |           |
| PhS4          | M I L D A | D Y I T E E G K P V I R L F | K K E N G E F K V E Y D R N                 | F R P Y I                         | A L L R D D S Q I D E V R K K I T | A E R H G |
| PhS5          | M I L D A | D Y I T E D G K P I I R L F | K K E N G E F K V E Y D R N                 | F R P Y I                         | A L L R D D S Q I D E V K K I T   | A E R H G |
| PhS6          | M I L D A | D Y I T E D G K P I I R L F | K K E N G E F K V E Y D R N                 | F R P Y I                         | A L L R D D S Q I D E V K K I T   | A E R H G |
| PhS7          | M I L D A | D Y I T E D G K P I I R L F | K K E N G E F K V E Y D R N                 | F R P Y I                         | A L L R D D S Q I D E V K K I T   | A E R H G |

Pfu  
DeepVent  
Hybrid\_design  
HyS1  
Hyb2  
Hyb3  
HyS4  
PhS1  
PhS2  
PhS3  
PhS4  
PhS5  
PhS6  
PhS7

[illegible]

pfu DeepVent Hybrid\_design HyS1 Hyb2 Hyb3 HyS4 PhS1 PhS2 PhS3 PhS4 PhS5 PhS6 PhS7

|               | 130         | 140     | 150        | 160    | 170  | 180        |
|---------------|-------------|---------|------------|--------|------|------------|
| Pfu           | LIDKGLIPMEG | EEEEELK | ILAFDIETLY | HEGEEF | GKGP | IIMISYADEN |
| DeepVent      | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| Hybrid_design | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| HyS1          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| Hyb2          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| Hyb3          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| HyS4          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| PhS1          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| PhS2          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| PhS3          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| PhS4          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| PhS5          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| PhS6          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |
| PhS7          | LIDKGLIPMEG | EEEEELK | LLAFDIETLY | HEGEEF | AKGP | IIMISYADEN |

|               | 190        | 200    | 210      | 220        | 230  | 240  |
|---------------|------------|--------|----------|------------|------|------|
| Pfu           | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| DeepVent      | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| Hybrid_design | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| HyS1          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| Hyb2          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| Hyb3          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| HyS4          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| PhS1          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| PhS2          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| PhS3          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| PhS4          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| PhS5          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| PhS6          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |
| PhS7          | VEVSSSEREM | IKRFLR | IIREKDPD | IIIVTYNGDS | SFDF | PYLA |

|               |      |     |      |     |     |     |    |     |    |    |   |    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------|------|-----|------|-----|-----|-----|----|-----|----|----|---|----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pfu           | 250  | 260 | 270  | 280 | 290 | 300 |    |     |    |    |   |    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| DeepVent      | GDMT | AV  | EV   | KGR | I   | HFD | LY | HV  | I  | TR | T | I  | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | K | A | W | E |   |   |
| Hybrid_design | GDMT | AV  | EV   | KGR | I   | HFD | LY | HV  | I  | RR | T | I  | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | H | E | I | A | E | A | W | E |   |   |
| HyS1          | MQR  | I   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | RR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | X | E | I | A | E | A | W | E |
| Hyb2          | MQR  | L   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | SR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | I | A | E | A | W | E |   |
| Hyb3          | MQR  | L   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | SR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | G | A | W | E |
| HyS4          | MQR  | L   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | SR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | G | A | W | E |
| PhS1          | MQR  | I   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | RR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | K | A | W | E |
| PhS2          | MQR  | I   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | RR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | H | E | I | A | E | A | W | E |
| PhS3          | MQR  | L   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | RR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | H | E | I | A | K | A | W | E |
| PhS4          | MQR  | I   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | TR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | E | A | W | E |
| PhS5          | MQR  | I   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | TR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | E | A | W | E |
| PhS6          | MQR  | I   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | TR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | E | A | W | E |
| PhS7          | MQR  | I   | GDMT | AV  | EV  | KGR | I  | HFD | LY | HV | I | TR | T | I | N | L | P | T | Y | T | L | E | A | V | Y | E | A | I | F | G | K | P | K | E | K | V | Y | A | D | E | I | A | E | A | W | E |

|               |      |     |     |     |     |     |     |     |     |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pfu           | 310  | 320 | 330 | 340 | 350 | 360 |     |     |     |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| DeepVent      | LERV | AKY | S   | MED | AKA | T   | Y   | E   | L   | G   | K   | E | F | L | P | M | E | I | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |   |
| Hybrid_design | LERV | AKY | S   | MED | AKV | T   | Y   | E   | L   | G   | R   | E | F | F | P | M | E | A | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |   |
| HyS1          | TG   | K   | G   | L   | ER  | V   | AKY | S   | MED | AKX | T   | Y | E | L | G | X | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |
| Hyb2          | TG   | K   | G   | L   | ER  | V   | AKY | S   | MED | AKA | T   | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |
| Hyb3          | TG   | E   | D   | L   | ER  | V   | AKY | S   | MED | AKA | T   | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |
| HyS4          | TG   | E   | D   | L   | ER  | V   | AKY | S   | MED | AKA | T   | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |
| PhS1          | TG   | E   | D   | L   | ER  | V   | AKY | S   | MED | AKA | T   | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |
| PhS2          | TG   | E   | D   | L   | ER  | V   | AKY | S   | MED | AKA | T   | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |   |
| PhS3          | S    | G   | E   | G   | L   | ER  | V   | AKY | S   | MED | AKA | T | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |
| PhS4          | S    | G   | E   | G   | L   | ER  | V   | AKY | S   | MED | AKV | T | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |
| PhS5          | S    | G   | K   | N   | L   | ER  | V   | AKY | S   | MED | AKA | T | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |
| PhS6          | S    | G   | K   | N   | L   | ER  | V   | AKY | S   | MED | AKA | T | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |
| PhS7          | S    | G   | K   | N   | L   | ER  | V   | AKY | S   | MED | AKA | T | Y | E | L | G | K | E | F | F | Q | L | S | R | L | V | G | Q | P | L | W | D | V | S | R | S | S | T | G | N | L | V | E | W | F | L | L | R | K |

|               |     |        |        |    |     |         |     |    |        |    |      |     |    |    |    |      |    |    |     |     |
|---------------|-----|--------|--------|----|-----|---------|-----|----|--------|----|------|-----|----|----|----|------|----|----|-----|-----|
| Pfu           | 370 | AYERNE | VAPNKP | SE | EYQ | RRRLRES | YTG | GG | FVKEPE | KG | LWEN | IVY | LD | FR | AL | YPS  | II | TH | NVS | 420 |
| DeepVent      |     | AYERNE | LAPNKP | DE | EY  | RRRLRES | YAG | GG | YVKEPE | KG | LWEG | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| Hybrid_design |     | AYERNE | LAPNKP | XE | YX  | RRRLRES | YX  | GG | XVKEPE | KG | LWES | XV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| HyS1          |     | AYERNE | LAPNKP | YE | Y   | RRRLRES | YTG | GG | FVKEPE | KG | LWES | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| Hyb2          |     | AYERNE | LAPNKP | AE | Q   | RRRLRES | YTG | GG | FVKEPE | KG | LWED | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| Hyb3          |     | AYERNE | LAPNKP | AE | Q   | RRRLRES | YTG | GG | FVKEPE | KG | LWED | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| HyS4          |     | AYERNE | LAPNKP | AE | Q   | RRRLRES | YTG | GG | FVKEPE | KG | LWED | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| PhS1          |     | AYERNE | LAPNKP | DE | EY  | RRRLRES | YAG | GG | FVKEPE | KG | LWEN | IVY | SL | DF | RS | LYPS | II | TH | NVS |     |
| PhS2          |     | AYERNE | LAPNKP | SE | EY  | RRRLRES | YTG | GG | FVKEPE | KG | LWEN | IVY | SL | DF | RS | LYPS | II | TH | NVS |     |
| PhS3          |     | AYERNE | VAPNKP | SE | EY  | RRRLRES | YAG | GG | YVKEPE | KG | LWEN | IVY | SL | DF | RS | LYPS | II | TH | NVS |     |
| PhS4          |     | AYERNE | VAPNKP | DE | EY  | RRRLRES | YTG | GG | YVKEPE | KG | LWEN | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| PhS5          |     | AYERNE | VAPNKP | DE | EY  | RRRLRES | YTG | GG | YVKEPE | KG | LWEN | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| PhS6          |     | AYERNE | VAPNKP | DE | EY  | RRRLRES | YTG | GG | YVKEPE | KG | LWEN | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |
| PhS7          |     | AYERNE | VAPNKP | DE | EY  | RRRLRES | YTG | GG | YVKEPE | KG | LWEN | LV  | SL | DF | RS | LYPS | II | TH | NVS |     |

|               |     |     |    |    |    |   |    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |
|---------------|-----|-----|----|----|----|---|----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|
| Pfu           | 430 | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L | 480 |
| DeepVent      |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| Hybrid_design |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| HyS1          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| Hyb2          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| Hyb3          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| HyS4          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| PhS1          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| PhS2          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| PhS3          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| PhS4          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| PhS5          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| PhS6          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |
| PhS7          |     | PDT | LN | EG | CK | N | YD | I | A | P | Q | V | G | H | K | F | C | K | D | I | P | G | F | I | P | S | L | L | G | H | L | L | E | E | R | Q | K | I | K | T | K | M | K | E | T | Q | D | P | I | E | K | I | L | L |     |

Pfu  
DeepVent  
Hybrid\_design

Pfu  
DeepVent  
Hybrid\_design

|               | 610                         | 620                         | 630            | 640 | 650 |
|---------------|-----------------------------|-----------------------------|----------------|-----|-----|
| pfu           | EGKVITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | QKLANVYEIIPPEK |     |     |
| DeepVent      | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| Hybrid_design | EGKVITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | QKLANVYEIIPPEK |     |     |
| HyS1          | EGKVITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | QKLANVYEIIPPEK |     |     |
| Hyb2          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| Hyb3          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| HyS4          | EGKVITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | QKLANVYEIIPPEK |     |     |
| PhS1          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| PhS2          | EGKVITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | QKLANVYEIIPPEK |     |     |
| PhS3          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| PhS4          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| PhS5          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| PhS6          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |
| PhS7          | EGKIITRGLEIVRRRDWSEIAKETQAR | VLEAII LKKGNDVEEAVRIIVKKEVI | TEKLSKVEIIPPEK |     |     |

|               | 670                    | 680  | 690      | 700   | 710          | 720            |                |
|---------------|------------------------|------|----------|-------|--------------|----------------|----------------|
| Pfu           | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAKKG   | GVKIK | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| DeepVent      | LVIYEQITRPLHEYKAIGPHVA | VAKK | LAAAGVVK | VR    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| Hybrid_design | LVIYEQITRPLHEYKAIGPHVA | VAKK | LAAAGVVK | XX    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| HyS1          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | IK    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| Hyb2          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | IK    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| Hyb3          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | IK    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| HyS4          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | IK    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| PhS1          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAKKG   | GVKIK | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| PhS2          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | IK    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| PhS3          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAKKG   | GVKIK | IR           | PGMVIGYIVLRG   | GGPISNRAILAAEE |
| PhS4          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | VR    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| PhS5          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | VR    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| PhS6          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | VR    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |
| PhS7          | LAIYEQITRPLHEYKAIGPHVA | VAKK | LAAARGVK | VR    | PGMVIGYIVLRG | GGPISNRAILAAEE |                |

Pfu  
DeepVent  
Hybrid\_design  
Hys1  
Hys2  
Hys3  
Hys4  
Phs1  
Phs2  
Phs3  
Phs4  
Phs5  
Phs6  
Phs7